When acute pancreatitis develops in a patient with primary nonpancreatic malignancy, conservative measures such as nasogastric tube suction, intravenous fluids, and the use of analgesics may be used first, and occasionally the pancreatitis may subside in a few days.[8,15,17] If clinical pancreatitis persists and a histologic diagnosis of pancreatic metastases has been made, systemic chemotherapy or abdominal irradiation should be considered in patients with small-cell carcinoma or lymphoma. Yeung and colleagues reported the cases of three patients with metastasis-induced acute pancreatitis associated with small-cell lung cancer, and clinical pancreatitis resolved completely two days, one week, and four weeks, respectively, after combination chemotherapy was instituted.[7] Levine and Danovitch reported the case of a patient with bronchogenic carcinoma-induced pancreatitis that did not respond to abdominal irradiation, whereas abdominal irradiation provided palliation in one of our patients with lymphoma (patient 5).

Acute pancreatitis due to metastasis seems to be an ominous prognostic sign in patients with primary nonpancreatic malignancy. Among those patients with survival data documented,[6-13,16,17,21,22] the vast majority died within six months after the diagnosis of acute pancreatitis. Only two patients with non-Hodgkin's lymphoma survived for more than six months.[16,17]

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Spontaneous Intracranial Hypotension

An Uncommon and Underrecognized Cause of Headache

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ALTHOUGH WELL DESCRIBED in the neurologic literature,[1-3] spontaneous intracranial hypotension (also called primary intracranial hypotension, primary cerebrospinal fluid hypotension, spontaneous hypoliquorrhea, and a number of other names) is generally not mentioned in reviews of headache diagnosis and treatment in the internal medicine literature.[4-6] We report a case of this headache disorder and review its characteristics, pathogenesis, and treatment.

Report of a Case

The patient, a 25-year-old woman with an unremarkable medical history, suddenly had moderate occipital and posterior cervical discomfort. She felt nauseated, vomited, and took a nap. On rising she had severe cervico-occipital pain—"the worst I ever felt in my life"—whenever she tried to sit or stand. When she lay down, she felt perfectly well, but she was essentially unable to stand or sit.

There was no history of fever or head trauma. The results of a general physical examination and the neurologic examination were within normal limits. A complete blood count with differential leukocyte count was normal. Magnetic resonance imaging (MRI) of the head showed the tips of the cerebellar tonsils to be within the foramen magnum.

A lumbar puncture was done with the patient in the lateral decubitus position. The opening pressure was 20 mm of cerebrospinal fluid (CSF). The CSF flowed from the needle slowly, but the flow rate increased with a Valsalva maneuver. The fluid was acellular, and protein and glucose concentrations were normal. No imaging study was done to look for an extradural CSF leak.

Treatment included a five-day course of corticosteroids, a high-salt diet, salt tablet supplements, and extra oral fluids. The headache was decreased at two weeks and gone in eight weeks.

Discussion

Headache is an extremely common outpatient problem with an extensive differential diagnosis. Most headaches, particularly in young people, are not the result of intracranial disease but are considered to represent tension or vascular headache, particularly if the headaches are chronic. The most common vascular headache is the common migraine; less common types include classic migraine, cluster headache, cough headache, exertional headache, and coitus-associated headache. New-onset and acute headaches raise

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ABBREVIATIONS USED IN TEXT

CSF = cerebrospinal fluid
MRI = magnetic resonance imaging

concern about the possibility of some serious intracranial disorder. Possibilities include infection (meningitis, encephalitis, or brain abscess), hemorrhage (subdural, subarachnoid, or intracerebral), and tumor (benign primary brain tumor, malignant primary brain tumor, or metastatic tumor).

Spontaneous intracranial hypotension is a type of new-onset headache with one essential clinical feature: prompt and striking relief of pain when the patient lies down, with prompt recurrence of pain on sitting or standing. This aspect of the headache is identical to that of the readily recognized post-lumbar puncture headache, but there has been no preceding lumbar puncture. A definitive diagnosis requires the demonstration of a low opening pressure when a lumbar puncture is done: the pressure should be less than 70 mm of CSF, perhaps less than 30 mm of CSF if the strictest diagnostic criterion is followed. The spinal fluid should flow freely with a Valsalva maneuver to confirm that the pressure reading accurately reflects intracranial pressure; if it does not, there may be a spinal block or the needle may be improperly placed. Sometimes there may actually be a negative opening pressure: a sucking sound can be heard when the stylet is withdrawn from the needle, and imaging studies may then show air in the subarachnoid space.

The headache is characteristically bilateral and variably posterior, holocranial, or anterior. Associated symptoms may include vertigo, nausea, vomiting, blurred vision, photophobia, neck stiffness, and occipitocervical pain with neck flexion. Confusion raises the question of bilateral subdural hematomas (sometimes occurring in this condition), whereas focal neurologic findings or seizures are rarely enough reported in this condition that other diagnoses should be considered.

Cerebrospinal fluid is often normal, but there may be increased protein (usually less than 1 gram per liter [100 mg per dl]) or an abnormal number of cells (particularly erythrocytes but sometimes leukocytes). The increased number of erythrocytes in the CSF could result from a number of causes: postulated hyperemia of the brain and meninges with diapedesis of erythrocytes into the CSF, mechanical disruption of bridging cortical veins by traction, and unrecognized traumatic lumbar puncture (particularly likely to occur in a patient with slow or no CSF flow from the needle.[1,2]

Brain imaging studies are usually normal; however, some patients may show bilateral subdural hematomas, caudal displacement of the cerebellar hemispheres and brain stem, or decreased size of the ventricles and basal cisterns. Subdural hematomas are thought to develop as the result of low CSF pressure rather than vice versa; traction on bridging cortical veins (because of a lack of buoyant support of the brain by the CSF) would be the most likely mechanism.

Bell and co-workers classified the intracranial hypotension syndromes into five types: primary or spontaneous, post-lumbar puncture, following head injury, following craniotomy, and as a result of severe intravascular volume depletion.[1] The spontaneous type and that following a craniotomy probably result from CSF leakage through a dural tear. The last type, severe intravascular volume depletion, could result from either decreased intracranial volume in the vascular compartment or decreased production of CSF by the choroid plexus.

The cause of the decreased intracranial pressure in the spontaneous syndrome is unknown, but there are three main hypotheses: hyposecretion, hyperabsorption, or leakage through a dural tear. Schaltenbrand (who first characterized this headache in 1938) considered it most likely that the decreased intracranial pressure was the result of a decreased rate of secretion of CSF by the choroid plexus.[7] Perhaps the strongest argument in favor of this hypothesis is the persistent CSF xanthochromia noted in some cases.[2] Isotope cisternography has provided some evidence to support the hypothesis of hyperabsorption,[3,8] but sometimes the clinical history,[9,10] clinical findings,[10] or radionuclide imaging[11] strongly support the concept of an extradural CSF leak. No one theory explains every feature of each case, and most likely this is a syndrome with a number of causes.

The mechanism of headache in intracranial hypotension is uncertain. Traction on pain-generating intracranial structures due to a lack of the buoyant effect of CSF on the brain has generally been postulated. Low intracranial pressure and CSF leaks do not always lead to the development of orthostatic headaches, however. When Marshall repeated lumbar punctures at 24 hours, CSF pressures of less than 60 mm occurred in 3 of 5 patients with positional headache and in 7 of 37 without headache ($P = .078$).[12] Clearly headache develops in some patients with low intracranial pressure and not in others, but the cause for this variability is unknown.

This patient had cerebellar tonsils that protruded into the foramen magnum, suggesting a Chiari I malformation. This malformation may present during adult life with a variety of symptoms including headache, diplopia, syncope, quadriparesis, or sensory abnormalities from associated syringomyelia. Low-lying cerebellar tonsils are being detected much more frequently now that head MRIs are commonly done, and it is probable that this patient's MRI findings were entirely coincidental. The possibility can be considered that her occipital headache developed from intracranial hypotension because of her low-lying cerebellar tonsils.

Most treatments have had as their rationale restoring normal CSF volume or eliminating a presumed CSF leak; without more definite knowledge of the pathogenesis of the syndrome, however, treatments may be regarded as empiric. Treatment efficacy is difficult to evaluate because the condition is self-limited and therapeutic regimens uncontrolled; there are reports of dramatic improvement with a variety of treatments. The simplest "treatment" is the avoidance of the upright position plus time. Systemic treatments postulated to help restore normal CSF volume have included inhalation of 5% carbon dioxide, increased oral fluid and salt intake, corticosteroid use,[2,13] and the intravenous administration of a normal saline solution. Intravenous caffeine and oral theophylline have been used primarily for post-lumbar puncture headache,[14,15] but the attempt has been made to use oral caffeine for the spontaneous syndrome.[3] Headaches have been relieved after single intrathecal injections of saline solution[2,16] and after continuous epidural saline infusions.[11,17] Epidural saline solution and epidural autologous blood "patching" have been postulated to eliminate extradural leakage of CSF, but Raskin has proposed that such therapy might be effective because of an indirect inactivation of adenosine receptors on cerebral blood vessels.[15] Epidural

autologous blood has been used primarily in patients with persistent post-lumbar puncture headache, but similar benefit has been noted in patients with spontaneous intracranial hypotension.[18,19]

Spontaneous intracranial hypotension needs to be considered when a patient presents with a new onset of headaches. In the absence of known causes of intracranial hypotension, the diagnosis is suggested by orthostatic headache and confirmed by lumbar puncture. This condition is generally benign and self-limited, but some patients require treatment of associated subdural hematoma or of persistent headache. Therapeutic modalities used have included increased oral fluid and salt intake, corticosteroids, caffeine, theophylline, intrathecal saline, epidural saline, and the use of autologous epidural blood "patching."

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